

REMARKS

This Amendment cancels pending claims 16, 19-22 and 28 in favor of new claims 31-36. The new claims correspond to the canceled claims, with method claim 31 being rewritten to recite affirmative method steps, which are supported at page 3, lines 6-12, page 6, lines 19-22 and page 21, line 20 to page 22, line 6. Claims 31-36 are pending.

This Amendment overcomes the 35 U.S.C. § 112, second paragraph, rejection of claims 16, 19-22 and 28. New claim 31 expressly defines acid dissociation constant as a negative logarithm, thereby removing the first ground for rejection.

With respect to the second rejection, *cis*-urocanic acid does in fact have a pKa value in the range of 6.7-7.4. The Patent Office cites page 116, right column, first sentence of Mohammad et al., 69 Photochemistry and Photobiology 115 (1999) as teaching that "urocanic acid" has pKa values of 3.5, 5.8 and 13. However, the very next sentence of Muhammad et al. teaching that *cis*-urocanic acid has pka values of 3.3 and 7.0, while *trans*-urocanic acid has pKa values of 4.0 and 6.0. Moreover, the applicants' specification also states *cis*-urocanic acid has a pKa value of 7.0 (Page 19, line 19).

Reconsideration and withdrawal of the indefiniteness rejections of claims 16, 19-22 and 28 are requested.

This Amendment overcomes the indefiniteness rejection of claims 19, 20 and 22. New claim 32 has been drafted in accordance with the Examiner's helpful interpretation of claim 19 (now canceled). Reconsideration and withdrawal of the indefiniteness rejection of claims 19, 20, and 22 are respectfully requested.

This Amendment also overcomes the 35 U.S.C. § 112, second paragraph, rejection of claims 16, 19-22 and 28 with respect to the term "non-dissociated form". New claims 31-36 do not use this phrase. Reconsideration and withdrawal of the indefiniteness rejection of claims 16, 19-22 and 28 are respectfully requested.

The 35 U.S.C. § 103(a) rejection of claims 16, 19, 20 and 28 over U.S. Patent No. 5,995,869 to Cormier et al. is traversed. The claimed method requires preparation of a pharmaceutical composition consisting essentially of an active substance consisting of a pharmaceutically acceptable agent or salt thereof capable of acidifying cell cytoplasm, with the agent being an acid having a dissociation constant, expressed as its negative logarithm pKa, in the range of 6.7 to 7.4. Cis-urocanic acid is a suitable agent.

Cormier et al. disclose skin sensitization in electrotransport drug delivery can be reduced or prevented by co-administering cis-uropic acid with a drug delivered via electrotransport (Col.5, lines 7-11). In contrast, the claimed method requires a composition whose active substance consists of a pharmaceutically acceptable acid having a dissociation constant, expressed as its negative logarithm pKa, in the range of 6.7 to 7.4, and which can acidify cell cytoplasm.

Cormier et al. fails to raise a prima facie case of obviousness against the claimed method because one of ordinary skill is given no motivation, suggestion or apparent reason to eliminate the drug to be delivered via electrotransport from the Cormier et al. composition. See In re Fitch, 972 F.2d 1260, 1265, fn. 12, 23 USPQ2d 17780, 1783 (Fed. Cir. 1992) (citing In re Gordon, 773 F.2d 900, 221 USPQ 1125 (Fed. Cir. 1984) for the proposition that a proposed modification is inappropriate for an obviousness inquiry when the modification renders the prior art reference inoperable for its intended purpose). In this case, omission of the drug from the Cormier et al. composition would render the Cormier et al. invention inoperable for its intended purpose - delivery of a drug to a patient via electrotransport.

Cormier et al. does not disclose or suggest that a composition whose active substance consists of a pharmaceutically acceptable acid having a dissociation constant, expressed as its negative logarithm pKa, in the range of 6.7 to 7.4, and adjusted to a pH of 6.1 to 7.0, can acidify cell cytoplasm and thereby treat a local inflammatory disease or disorder. Reconsideration and withdrawal of the obviousness rejection of claims 16, 19-22 and 28 over Cormier et al. are respectfully requested.

The 35 U.S.C. § 103(a) rejection of claims 21 and 22 over Cormier et al. in view of U.S. Patent 5,912,010 to Wille et al. is also traversed. As discussed above, the claimed method requires preparation of a pharmaceutical composition whose active substance consists of a pharmaceutically acceptable acid or salt thereof having a dissociation constant, expressed as its negative logarithm pKa, in the range of 6.7 to 7.4, and which is capable of acidifying cell cytoplasm.

The cited combination of references fails to raise a prima facie case of obviousness against the claimed method because one of ordinary skill in the art is given no motivation or suggestion to modify Cormier et al. by omitting the drug to be delivered via electrotransport from its composition. Reconsideration and

withdrawal of the obviousness rejection of claims 21 and 22 over Cormier et al. in view of Wille et al. are requested.

It is believed this application is in condition for allowance. Reconsideration and withdrawal of all rejections of claims 16, 19-22 and 28, and issuance of a Notice of Allowance directed to claims 31-36, are earnestly requested. The Examiner is urged to telephone the undersigned should he believe any further action is required for allowance.

The extension of time fee is being paid electronically today. It is not believed any additional fee is required for entry and consideration of this Amendment. Nevertheless, the Commissioner is authorized to charge Deposit Account No. 50-1258 in the amount of any such required fee.

Respectfully submitted,

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Enclosure:
Petition for Extension of Time